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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,722	10/23/2003	Jerome B. Zeldis	9516-078-999	2389

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222 EAST 41ST ST
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EXAMINER	
OLSON, ERIC	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
09/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,722	ZELDIS ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9,23 and 27-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9,23 and 27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted July 9, 2007 wherein the rejections of record in the previous office action are traversed. This application claims benefit of provisional application 60/421004, filed October 24, 2002.

Claims 1-5, 9, 23, and 27-34 are pending in this application.

Claims 1-5, 9, 23, and 27-34 as amended are examined on the merits herein.

Applicant's remarks, submitted July 9, 2007, with respect to the rejection of instant claims 1, 2, 9, and 27-34 under 35 USC 102(e) as being anticipated by Schafer et al., have been fully considered and found to be persuasive to remove the rejection because the priority claim to provisional application 60366515 made by Schafer et al. does not provide support for a method of treating complex regional pain syndrome. Thus Schaffer is not prior art under 35 USC 102(e). Therefore the rejection is withdrawn.

Applicant's remarks, submitted July 9, 2007, with respect to the rejection of instant claims 3-5 and 23 under 35 USC 103(a) as being anticipated by Schafer et al. in view of Merck, have been fully considered and found to be persuasive to remove the rejection as the claimed subject matter of Schafer et al. was commonly owned by Celgene Corporation at the time of the invention, and Schaffer is not prior art under 35 USC 102(e) as discussed above. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 9, and 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omoigui (US patent publication 20040038874, of record in previous action) in view of Muller et al. (US patent 6020358, of record in previous action) Omoigui discloses a method for the treatment of persistent pain by administering a drug that antagonizes one or more mediators of inflammation. (p. 1, paragraph 0004) Drugs useful in this manner include TNF-α blockers (p. 2, paragraphs 0007 and 0011) including thalidomide and thalidomide analogs. (p. 3, paragraph 0023) Reflex Sympathetic Dystrophy, otherwise known as chronic regional pain syndrome, is listed as a disease treatable by this method. (pp. 9-10, paragraphs 0078-0082) Omoigui does not disclose a therapeutic method comprising administering the specific TNF-α inhibitor (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione, or one involving a pharmaceutical dosage form having the specific limitations of instant claims 28-34.

Muller et al. discloses that compounds of a general formula including that of the claimed compound (column 5, line 1) are capable of decreasing the levels of TNF-α in a patient, (column 4, lines 55-67) thus qualifying as a TNF-α blocker. Example 12

(column 14, lines 35-55) is the exact same compound (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione disclosed in the instant claims. Muller et al. also discloses oral dosage forms of this compound as tablets or capsules, having a unit dosage of 1-100 mg, along with another dosage form in isotonic saline, a pharmaceutically acceptable solvate. (column 9, lines 22-52)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the compound of example 12 of Muller et al. in the method of Omoigui, in an appropriate dosage form as disclosed by Muller et al. One of ordinary skill in the art would have been motivated to use this compound and dosage form because it is disclosed by Muller et al. to be useful for lowering TNF-α levels in a subject. One of ordinary skill in the art would reasonably have expected success because the scope of Omoigui includes all compounds capable of inhibiting or otherwise blocking the activity of TNF-α.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted July 9, 2007, have been fully considered as regards the above grounds of rejection and not found to be persuasive to remove the rejection. Applicant argues that substantial difference exist between the claimed subject matter and the prior art, and goes on to argue that each of the references discloses an invention different from that of the instant claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA

1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the references in combination teach or suggest every element of the instant claims, and therefore the fact that neither reference individually discloses all of the elements of the instant claims does not indicate nonobviousness.

Applicant further argues that no reason has been provided that one of ordinary skill in the art would have combined the references. In the instant case, as discussed above, the fact that Muller et al. discloses that the claimed compound is a TNF-alpha inhibitor would clearly motivate one of ordinary skill in the art to use this compound to use this compound in the method of Omogui in view of Omogui's teaching that TNF-alpha inhibitors are useful for treating pain, such as CRPS. In other words, Muller et al. clearly discloses the compound of the instant claims as a species of the broad genus of compounds useful in the method of Omogui. This is a sufficient motivation for combining the references, since one of ordinary skill in the art would have known that they could be successfully used in this method. Where two elements are known to have the same function, substituting one for the other, as is the case herein where one TNF-alpha inhibitor is substituted for another, is an obvious modification of the prior art that can be easily and predictably by anyone of ordinary skill in the art.

Furthermore, the compounds of Muller et al. possess a phthalimide moiety that is the same as the phthalimide moiety of thalidomide. (See figure 1 below) This structure is sufficiently close in structure to the thalidomide derivatives disclosed by Omogui that it would be expected to have similar utility given it's shared activity as a TNF-alpha inhibitor. This structural similarity further indicates that the claimed compound is

expected to function as a "thalidomide derivative" in the method of Omogui, providing an additional reason to combine the references. Therefore the rejection is maintained and made **FINAL**.

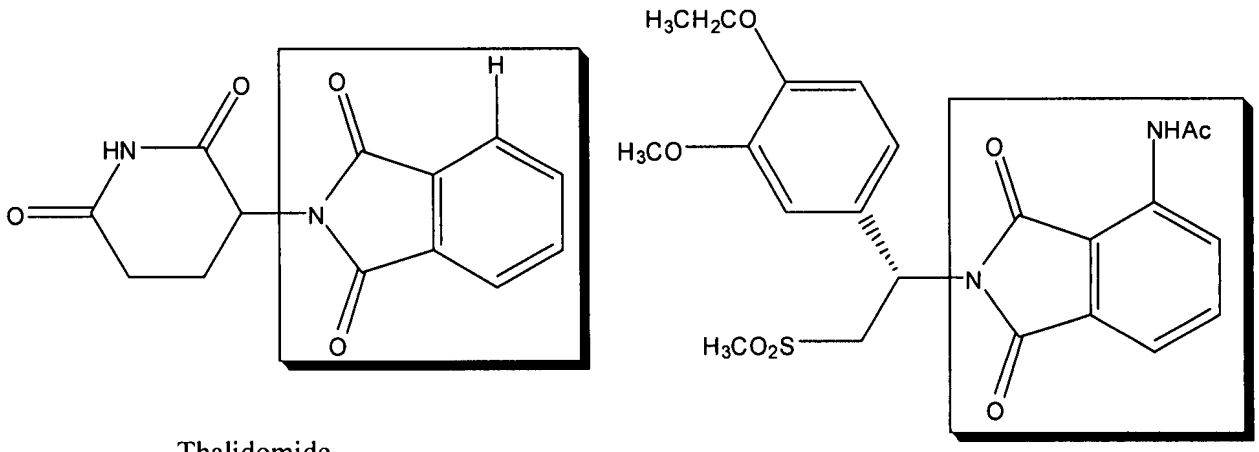

Figure 1 - The claimed compound shares a phthalamide moiety with thalidomide and is expected to possess similar utility to the "thalidomide derivatives" of Omoigui.

Claims 2-5 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omoigui (US patent publication 20040038874, of record in previous action) in view of Muller et al. (US patent 6020358, of record in previous action) as applied to claims 1, 9, and 27-34 above, and further in view of Merck. (Reference of record in previous office action) The disclosure of Omoigui in view of Muller et al. is discussed above. Omoigui in view of Muller et al. does not disclose a method further comprising administering the additional therapeutic agents of instant claims 2-5 or the therapies of instant claim 23.

Merck discloses that complex regional pain syndrome may be treated with several drugs including nifedipine, prednisone, opioid analgesics, tricyclic

antidepressants, and anticonvulsants. (p. 1373, left column, second paragraph) It should be noted that it is well known in the art that opioid analgesics include oxycodone, tricyclic antidepressants include amitryptyline, imipramine, and doxepin, and anticonvulsants include gabapentin. Merck also discloses that physical therapy is essential throughout therapy for complex regional pain syndrome (p. 1373, left column, last paragraph) and that pain relief that outlasts the administration of a sympathetic block but is still transitory suggests the need for surgery. (p. 1373, left column, second paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of Omoigui et al. for the treatment of complex regional pain syndrome further comprising administering one or more of the pharmaceutical active agents described by Merck and still further administering physical therapy and/or surgery. One of ordinary skill in the art would have been motivated to combine these teachings because Omoigui et al. and Merck both disclose their respective teaching as being useful for treating the same condition, namely complex regional pain syndrome. One of ordinary skill in the art would reasonably have expected success because combining two treatments known in the prior art to be effective for treating the same disorder by different methods is reasonably expected to produce at least additive effects.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted July 9, 2007, have been fully considered as regards the above grounds of rejection and not found to be

persuasive to remove the rejection. Applicant argues that substantial difference exist between the claimed subject matter and the prior art, and goes on to argue that each of the references discloses an invention different from that of the instant claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the references in combination teach or suggest every element of the instant claims, and therefore the fact that neither reference individually discloses all of the elements of the instant claims does not indicate nonobviousness.

Applicant further argues that no reason has been provided that one of ordinary skill in the art would have combined the references. In the instant case, as discussed above, the fact that Muller et al. discloses that the claimed compound is a TNF-alpha inhibitor would clearly motivate one of ordinary skill in the art to use this compound to use this compound in the method of Omogui in view of Omogui's teaching that TNF-alpha inhibitors are useful for treating pain, such as CRPS. In other words, Muller et al. clearly discloses the compound of the instant claims as a species of the broad genus of compounds useful in the method of Omogui. This is a sufficient motivation for combining the references, since one of ordinary skill in the art would have known that they could be successfully used in this method. Where two elements are known to have the same function, substituting one for the other, as is the case herein where one TNF-

alpha inhibitor is substituted for another, is an obvious modification of the prior art that can be easily and predictably by anyone of ordinary skill in the art.

Furthermore, the compounds of Muller et al. possess a phthalimide moiety that is the same as the phthalimide moiety of thalidomide. (See figure 1 above) This structural similarity further indicates that the claimed compound is expected to function as a "thalidomide derivative" in the method of Omogui, providing an additional reason to combine the references. Therefore the rejection is maintained and made **FINAL**.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over either claims 1, 6, 12, and 17 of U.S.

Patent No. 6020358 (Reference cited in PTO-1449 July 26, 2004, herein referred to as '358) or alternately claims 1, 4, 10, and 15 of U.S. Patent No. 6011050 (Reference cited in PTO-1449 July 26, 2004, herein referred to as '050) in view of Omoigui. (US patent publication 20040038874, cited in PTO-1449 July 26, 2004 July 26, 2004) Claim 17 of '358 and claim 15 of '050 are both drawn to methods of reducing undesirable levels of TNF-α in a mammal by administering a compound having a generic structure which includes within its breadth the species recited in instant claim 27. Claims 6 and 12 of '358 and 4 and 10 of '050 further suggest the claimed structure by defining R4, R5, and R6. Said claims do not disclose a method of treating neuropathic pain in this manner.

Omoigui discloses a method for the treatment of persistent pain by administering a drug that antagonizes one or more mediators of inflammation. (p. 1, paragraph 0004) Drugs useful in this manner include TNF-α blockers. (p. 2, paragraphs 0007 and 0011) Reflex Sympathetic Dystrophy, otherwise known as chronic regional pain syndrome, is listed as a disease treatable by this method. (pp. 9-10, paragraphs 0078-0082)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the methods of Claim 17 of '358 and claim 15 of '050 on a mammal suffering from neuropathic pain caused by a herniated disk. One of ordinary skill in the art would have been motivated to practice the invention in this manner because claims 1, 21, and 27 of '250 disclose that blocking the action of TNF-α is an effective strategy for treating neuropathic pain in a herniated disk. One of ordinary skill in the art would have reasonably expected success because claims 1, 21, and 27 of '250 already demonstrate the utility of this method.

Response to Argument: Applicant's arguments, submitted July 9, 2007, have been fully considered as regards the above grounds of rejection and not found to be persuasive to remove the rejection. Applicant argues that the aforementioned claims merely claim a genus without specifically claiming the individual species of the instant claims. However, according to MPEP 2131.02, "When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be "at once envisaged." One may look to the preferred embodiments to determine which compounds can be anticipated. In re Petering, 301 F.2d 676, 133 USPQ 275 (CCPA 1962)." In the instant case, one of ordinary skill in the art would have clearly envisaged the claimed compound from the genus of claim 1 of '050, in view of the further limitations provided in dependent claims 4, 10, and 12 of '050, which limit the genus to a narrow genus having only a few well-defined embodiments. These dependent claims are preferred embodiments which would aid one of ordinary skill in the art in selecting the compound of the instant claims from the genus of '050. IN the case of US patent

6020358, claims 2, 6, 12, and 14 similarly disclose a narrow preferred subgenus from which the claimed species can be at once envisaged.

Therefore the rejection is deemed proper and made **FINAL**.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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